

Application No.: 10/572,404
Filing Date: March 16, 2006

REMARKS

This Response after final is responsive to the questions raised by the Examiner in the Final Office Action regarding discrepancies between the 132 Declarations of May 15, 2008 and April 30, 2009, both Declarations of Miyuki Tanaka. Applicants submit herewith a new 132 Declaration of Miyuki Tanaka to address these questions.

In a brief telephonic interview on September 15, 2009, the Examiner kindly agreed to consider such 132 Declaration directed to an explanation of what she had viewed as discrepancies between the May 15, 2008 Declaration and the April 30, 2009 Declaration.

Rejection under 35 U.S.C. § 102(b)

Claim 18 remains rejected under 35 U.S.C. § 102 (b) as being anticipated by Ajabnoor (Journal of Ethnopharmacology 28: 215-220, 1990) as evidenced by Tanaka, et al. (Biol. Pharm. Bull. 29(7): 1418-1422, 2006).

Present claim 18 is directed to methods of improving hyperglycemia by administering 9,19-cyclolanostan-3-ol at a concentration of 0.001 to 10% by dry mass. The cited reference, Ajabnoor, teaches administration of a "bitter principle" from an extract of *Aloe barbadensis* leaves. Applicants previously presented a Declaration from inventor Miyuki Tanaka (April 30, 2009) which shows that "bitter principle" of Ajabnoor contains no 9,19-cyclolanostan-3-ol.

The Examiner questioned this conclusion in light of an earlier Declaration of Miyuki Tanaka (May 15, 2008) which indicated the presence of a certain level of 9,19-cyclolanostan-3-ol in the Aloe vera plant. Applicants assert that the conclusions of the April 30, 2009 132 Declaration do NOT conflict with the conclusions of the May 15, 2008 132 Declaration. In brief, the extracts of the May 15, 2008 132 Declaration were prepared from a different part of the Aloe vera leaf than the extracts of the April 30, 2009 Declaration as explained in more detail below and in the attached new 132 Declaration (the present 132 Declaration). Reference is made to the attached Figure 1 from US Patent No.4,735,935, which illustrates the three basic components of the Aloe vera leaf and to the attached photo (which will also be sent to the Examiner by email so that the color differences may be appreciated).

As described in the present Declaration and illustrated in Figure 1 of U.S. Patent No. 4,735,935, the Aloe leaf can be divided into three (3) portions, the inner clear gel (1), a yellow liquid that is present between the rind and the inner clear gel (brownish-red when dry) (2) and the rind (cortex) (3). This numbering corresponds to the numbering used in U.S. Patent No. 4,735,935. Parts 1 and 2 are also present in the attached illustration (color version sent by email). In the photo, the left side is portion 1 and the right side is portion 2.

Yellow liquid is present in portion 2 which will ooze out or drain when leaf is cut. When dried, this yellow liquid is a brownish-red color, bitter in taste and known as "Aloes". This is also explained in column 1 of U.S. Patent No. 4,735,935.

Portion 1 contains a gel that does not flow out when the leaf is cut and is referred to in the art as "Aloe vera".

Ajabnoor

In view of the above explanation, it is apparent that the teaching of Ajabnoor refers to portion 2 of the Aloe leaf (see 2nd sentence of Introduction on page 215 of Ajabnoor). As described in the previous Tanaka Declaration of April 30, 2009, this portion (the bitter principle, Portion 2) prepared by ethyl acetate extraction of *Aloe* leaves contains no 9,19-cyclolanostan-3-ol.

As stated in Applicants' specification at page 17, paragraph 4, 9,19-cyclolanostan-3-ol is contained in the **clear gel of portion 1** of the Aloe leaf. Applicants teach either whole leaf or portion 1 as source material, preferably portion 1. As stated at page 17, paragraph 4, "...although the whole of the aforementioned plant may be used, it is preferable to use mesophyll (clear gel portion) thereof". Accordingly, Applicants prepare 9,19-cyclolanostan-3-ol from portion 1 of the *Aloe vera* plant whereas Ajabnoor uses portion 2, which is consistent with the differences reported in presence / absence of 9,19-cyclolanostan-3-ol in the April 30, 2009 132 Declaration.

May 15, 2008 Declaration

The May 15, 2008 Declaration pertains to the Aloe vera juice of Yongchaiyudha which is from Portion 1 of the Aloe leaf. Yongchaiyudha teaches Aloe vera juice obtained by squeezing Aloe gel (Portion 1). Although this juice does contain 9,19-cyclolanostan-3-ol, the amount is

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much less than the compositions of Applicants' claim 18 which comprises 0.001 to 10% by dry mass. Yongchaiyudha does not teach enriching the Aloe vera juice in 9,19-cyclolanostan-3-ol.

Conclusion

In view of Applicants' explanation above, it is respectfully requested that the Examiner reconsider the 132 Declaration with respect to the Ajabnoor reference. Applicants again assert that Ajabnoor cannot anticipate the claimed invention as their extracts do not contain 9,19-cyclolanostan-3-ol. This finding is not inconsistent with the previous Declaration (May 15, 2008) as discussed above and in the attached present 132 Declaration.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

Co-Pending Applications of Assignee

Applicant refers to the Amendment submitted May 15, 2008 which lists co-pending applications of Assignee.

CONCLUSION

In view of the present 132 Declaration and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the

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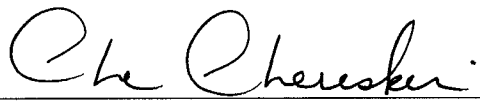
Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: Oct. 7, 2009

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PHOTO ATTACH MENT



United States Patent [19]

McAnalley

[11] Patent Number: 4,735,935
[45] Date of Patent: Apr. 5, 1988

- [54] PROCESS FOR PREPARATION OF ALOE PRODUCTS, PRODUCED THEREBY AND COMPOSITIONS THEREOF
- [75] Inventor: Bill H. McAnalley, Grand Prairie, Tex.
- [73] Assignee: Carrington Laboratories, Inc., Dallas, Tex.
- [21] Appl. No.: 869,261
- [22] Filed: Jun. 5, 1986

Related U.S. Application Data

- [63] Continuation-in-part of Ser. No. 810,025, Dec. 17, 1985, abandoned, which is a continuation-in-part of Ser. No. 754,859, Jul. 12, 1985, abandoned, which is a continuation-in-part of Ser. No. 750,321, Jun. 28, 1985, abandoned, which is a continuation-in-part of Ser. No. 649,967, Sep. 12, 1984, abandoned, which is a continuation-in-part of Ser. No. 375,720, May 7, 1982, abandoned.
- [51] Int. Cl.⁴ A61A 31/715
- [52] U.S. Cl. 514/53; 514/54; 514/847; 424/DIG. 13; 536/53; 536/123
- [58] Field of Search 514/53, 54, 847; 536/1.1, 53, 123; 424/DIG. 13

[56] References Cited

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(List continued on next page.)

Primary Examiner—J. R. Brown
Assistant Examiner—John W. Rollins
Attorney, Agent, or Firm—Hubbard, Thurman, Turner & Tucker

[57] ABSTRACT

Process for producing aloe extracts including the separation of the leaves of the aloe plant into distinct portions. In particular, a first process is described for producing an aloe extract which is substantially free of anthraquinone-rich yellow sap and a second process is described for extracting the active chemical substance in the aloe plant.

The active chemical substance in the aloe plant is extracted from aloe leaves and its characteristic properties are described.

5 Claims, 28 Drawing Sheets

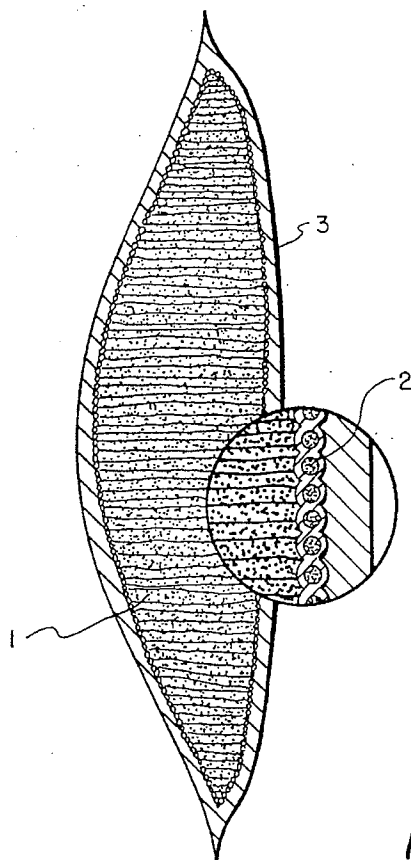


FIG. 1

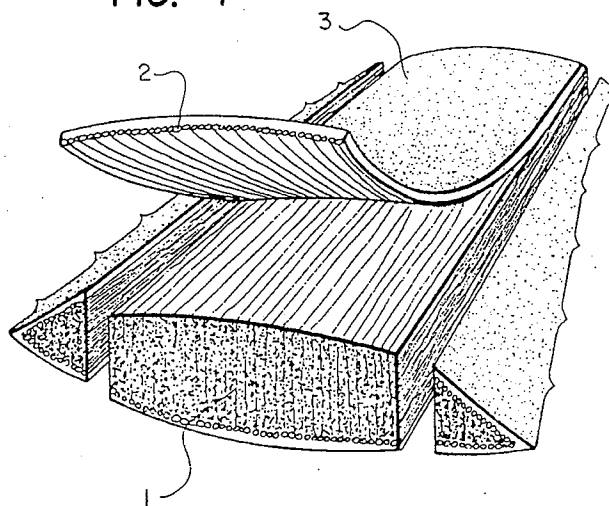


FIG. 2

PROCESS FOR PREPARATION OF ALOE PRODUCTS PRODUCED THEREBY AND COMPOSITIONS THEREOF

RELATED APPLICATIONS

This application is a continuation-in-part of an application filed Dec. 17, 1985, Ser. No. 810,025, now abandoned, which is a continuation-in-part of an application filed July 12, 1985, Ser. No. 754,859, now abandoned, which is a continuation-in-part of an application filed June 28, 1985, Ser. No. 750,321, now abandoned, which is a continuation-in-part of an application filed Sept. 12, 1984, Ser. No. 649,967, now abandoned, which is a continuation of an application filed May 7, 1982, Ser. No. 375,720, now abandoned. Said application Ser. No. 810,025 being entitled "Processes for Preparation of Aloe Products and Products Produced Thereby". Said applications Ser. Nos. 754,859; 750,321; 649,967; and 375,720 being entitled "Process for Preparation of Aloe Vera Products".

BACKGROUND OF THE INVENTION

1. Field of the Invention

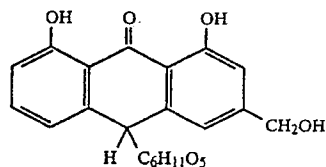
This invention pertains to the field of processing aloe plants and removing portions of said plant for processing same into compositions for topical and internal applications, and compositions of matter comprising said portions of aloe.

2. Description of the Prior Art, and Other Information

Approximately 325 species of Aloe are known, and most are indigenous to Africa. *Aloe barbadensis* is native to northern Africa, and was introduced into the island of Barbados about 1630. A variety of *Aloe barbadensis* (called *Aloe chinensis* Baker) was introduced by William Anderson into Curacao in 1817 from China. It was cultivated in Barbados for its laxative fraction until the middle of the nineteenth century, when the industry began to wane. Curacao aloe, which is often called Barbados aloe, comes from the Dutch islands of Aruba and Bonaire. The market for laxative aloe diminished as better and safer laxatives were developed.

The plant contains two separate juice materials. One is made from the clear cellular gel and the second, a yellow juice, is contained in the pericyclic cells of the vascular bundles located at the junction between the rind (cortex) and the internal fillet (FIGS. 1 and 2—1 is the clear cellular gel, 2 the yellow juice containing anthraquinones, 3 is the rind).

For centuries the yellow juice has been dried and used as a laxative. For example, in the Dutch islands of Aruba and Bonaire, leaves are cut in March and April, then placed cut end downward on a V-shaped trough which is inclined so that the latex can be fed into a cooking vessel. Varro E. Tyler, PHARMACOGNOSY at pp. 60-63 (Lea and Febiger, Philadelphia, 1981). The dried latex of the leaves of *Aloe barbadensis* Miller or other Aloes ranges in color from reddish-black to brownish-black to dark brown in color. The taste of each variety of dried latex is nauseating and bitter; also the odor is characteristic and disagreeable. It contains a number of anthraquinone glycosides; the principal one is called barbaloin (aloe-emodin anthrone C-10 glucoside). This dried latex, that has been sold for centuries as a laxative, is commonly called aloe or aloes.



(±) Barbaloin

The active laxative constituents vary quantitatively and qualitatively according to the species and environmental growing conditions. For example, Curacao aloe contains two and one half times as much aloe-emodin when compared to Cape Aloe, and Curacao aloe contains an appreciable amount of free chrysophanic acid not present in other types of aloe (Tyler, op. cit.). Many companies sell Aloe products that contain a large amount of the yellow sap even claiming them to be beneficial. Both juices become mixed together by the juice extraction process which is used by many producers.

The following species of Aloe have been used commercially for their yellow sap, which was dried and used as a laxative. Arthur Osol et al., THE UNITED STATES DISPENSATORY AND PHYSICIANS' PHARMACOLOGY, (J. B. Lippencott Co., Philadelphia, 1980) at pp. 42-43:

"1. *Aloe perryi* Baker.—The true Socotrine aloe is a perennial herb, growing abundantly on the island of Socotra especially in the limestone tracts, from the sea level to an altitude of 3,000 feet and also found in eastern Africa and in Arabia. It has a trunk one foot high which bears on its summit a dense rosette of pale green or reddish, succulent, lanceolate leaves with brown-tipped marginal spines.

"2. *Aloe barbadensis* Mill.—(*A. vera* "L"; *A. vulgaris* Lamarck).—This species, which is the source of Curacao aloe, has a very short, woody stem, and lanceolate embracing leaves, of glaucous green color, with hard, pale spines. It has bright yellow flowers arranged in a spicate inflorescence. *A. barbadensis* is a native of southeastern Europe, northern Africa, and Madagascar. It is cultivated in Italy, Sicily, Malta, and especially in the West Indies.

"3. *Aloe ferox* Miller, one of the three South African, tree-like species yielding Cape aloe, is one of the tallest species of the genus. [sic] It has a forked stem 5 to 15 feet long, 4 to 6 inches in diameter; furnished at the top with a dense rosette containing 30 to 50 lanceolate leaves 1.5 to 2 feet long, with prickles.

"4. *Aloe africana* Mill., an aborescent South African species, has a simple tall trunk which bears on its summit a few triangular-oblong, glaucous, green leaves with large, horny marginal teeth. It is a native of the Cape Colony.

"5. *Aloe spicata* Baker. (*A. Eru.* var. *cornuta* Berger) is a tall, branched aloe indigenous to tropical southern Africa. It possesses pale, glossy, fleshy leaves with white blotches and a panicle of campanulate yellow flowers."

The current status of the yellow sap portion of Aloe as a laxative is best summarized by the text of Goodman and Gilman, as follows:

"The yellow sap has not been subjected to controlled clinical comparison with the other anthraquinones but has the reputation of being the most irritating of these